# Uncertainty Factor Protocol for Ecological Risk Assessment
## **Toxicological Extrapolations to Wildlife Receptors**

***Approach***: *Select the "most applicable" published literature on field or laboratory studies of dose-responsive toxicity for each chemical contaminant of ecological concern (COC) and receptor of concern (ROC) combination. Obtain the categorical information below to properly extrapolate a selected study's toxicological design and findings to both chronic no-observable-adverse-effect-level (NOAEL) and low-observable-adverse-effect-level (LOAEL) doses as "toxicological reference values" (**TRV**). Use the extrapolated $TRV_{NOAEL}$ and $TRV_{LOAEL}$ to help develop a range (coupled with the 95% UCL C-term and with the CTE to RME exposure ranges) of dose-based hazard quotients (HQs), with the intent being that HQs <NOAELs pose no excess risk and HQs >LOAELs begin to pose more of a population risk. Note, that under this uncertainty factor (UCF) scheme, R8 toxicologists advise: quantitate HQs only if total UCFs are #100, report HQs as semi-quantitative (low, medium, or high hazards) when total UCFs are #500 but >100, and qualitatively (presence or absence) assess hazards if UCFs are >500. When faced with less-than-fully quantitative HQs, either attempt to do better literature searches or identify and conduct studies to fill data-gaps that will possibly reduce toxicological uncertainties. Tissue residue data (vs doses) are scarcer and usually less informative for extrapolations. Dietary concentrations must be converted to doses. Finally, EPA guidance and sound science dictate that TRV-based HQs must be professionally balanced and interpreted (spatial, temporal and population scales) with field effects data (which can also vary greatly in quality and relevance) to credibly assess ecological risk in terms of both excessiveness and reduction of exposure to achieve sufficient safety of local exposed populations.*

***TRV Goal** = Extrapolate to a chronic NOAEL with non-lethal toxicity for HQ development and to a chronic LOAEL as a HQ that relates more to impacts on population sustainability (incidence of effects per dose).*

| Basis for Uncertainty | Uncertainty Value Assigned |
|---|---|
| **A. Intertaxon** Variability Extrapolation Category | |
| Same species | 1 |
| Same genus, different species | 2 |
| Same family, different genus | 3 |
| Same order, different family | 4 |
| Same class, different order | 5 |
| Same phylum, different class | generally too far to extrapolate |
| **B. Exposure Duration** Extrapolation Category | |
| Chronic studies where toxicant attains pseudo-steady-state<br>- generally >30 days for aquatic species and reproductive endpoints, and usually >90 days for terrestrial species and other endpoints | 1 |
| Subchronic studies where toxicant has not attained steady-state<br>- generally $10 days for aquatic species and reproductive endpoints, and usually $30 days for terrestrial species and other endpoints | 3 |
| Subacute studies<br>- generally 4-9 days for aquatic species and reproductive endpoints, and usually 7-29 days for terrestrial species and other endpoints | 5 |
| Acute studies<br>-- usually 1-3 days for aquatic and 1-6 days for terrestrial | 10 (avoid) |
| Peracute studies -- usually <1 day and single exposures | 15 (don't use) |

| Basis for Uncertainty | *continued* | Uncertainty Value Assigned |
|---|---|---|

## C. **Toxicologic Endpoint** Extrapolation Category

Note: if reported, use the study's NOAEL and LOAEL for TRVs, else use the ratios below to estimate a non-lethal NOAEL and LOAEL from the study report of other endpoints; only use the NOEL and LOEL (non-toxic) adjustments "if" the study also looked for adverse (toxic) effects, else consider as O**A**ELs. Use professional ecotoxicologic judgement to decide on population importance of non-lethal severity.

| | | **Non-Lethal** | | | vs | Lethal |
|---|---|---|---|---|---|---|
| | | **mild** | | severe | | |
| No observed effects level | NOEL: | .75 | to | 1 | | 2 |
| No observed adverse effect level (.$ED_{01}$) | **NOAEL**: | 1 | to | 2 | | 3 |
| Lowest observed effects level | LOEL: | 2 | to | 3 | | 5 |
| Lowest observed adverse effects level (.$ED_{10}$) | **LOAEL**: | 3 | to | 5 | | 10 |
| Frank effects level (.$ED_{50}$) | FEL: | 5 | to | 10 | | 15 |

## D. **Modifying** Factor Category

Use professional ecotoxicological judgement to consider need for none, some or all modifiers, and give rationale (maximum deviations need definitive data); note that a value of "1" specifies no modification, and that these (up to 2-decimals) multipliers are combined with UCF divisors above to generate a TRV.

| | | | |
|---|---|---|---|
| Threatened, or listed, and endangered species<br>- L = 1.25, T = 1.5, E = 2 | 1 | to | 2 |
| Relevance of endpoint to ecological health<br>- population sustainability, incidence and severity | 1 | to | 2 |
| Extrapolating from lab to field or between<br>- relative reality of field conditions vs lab control | .5 | to | 2 |
| Study conducted with relevant co-contaminants<br>- *in situ* or test actual media vs ignore major interactants | .5 | to | 2 |
| Endpoint is mechanistically clear vs unclear<br>- plausibly applied to ROC vs less plausible effect | 1 | to | 2 |
| Study species is either highly sensitive or highly resistant<br>- if known, can adjust for ROC response | .5 | to | 2 |
| Ratios used to estimate whole body burden from tissue or egg<br>- mostly used for tissue residue comparisons | 1 | to | 2 |
| Intraspecific variability<br>- substantial susceptibility differences due to age, gender, developmental | 1 | to | 2 |
| Other applicable modifiers<br>- define and present convincing scientific evidence for adjustment | .5 | to | 2 |

-- **TRV = Study Dose ÷ Total UCFs**, Total UCFs = A x B x C x D, where D = $d_1$ x $d_2$ x $d_3$...x $d_n$

-- **To convert dietary concentrations into doses** for TRV development (kg food / kg BW-d), use study information if available, or EPA 1993 Exposure Factors Handbook values, or valid literature